REMARKS

Claims 3-6 and 9-10 have been canceled.

Claims 1, 2, 7, 8, 11-15 are currently pending and claims 1, 2, 7, 8 and 11-15 have been amended.

Support for the amendments to claim 1 can be found in the Specification at page 4, lines 3-4 and lines 19-20 and in the Examples.

Support for the amendments to claims 2 and 7 can be found in the Examples.

Claims 8 and 11-15 have been amended to reflect changes in the preamble of claim 1.

New claims 16-19 have been added. Support for the new claims can be found in the canceled claims and in the Examples section of the Specification.

New claims 20-23 find support in the Specification on page 3, lines 13-19, page 4, lines 9-15 and Example 10.

No new matter has been added.

Amendments to the Specification

Applicants have amended paragraph 6 of the Specification to recite that torasemide has a crystalline structure with a melting point of 163-164°C. The crystalline structure of torasemide and its melting point are inherent properties of the chemical, as can be seen by the attached copy of the description for torasemide (9690) in the Merck Index, the attached copy of the description of torasemide by DrugBank and the attached copy of the description of torasemide by Chemical Book. That torasemide is crystalline with a melting point of 163-164°C is also supported by US 4,018,929, which is cited in paragraph 6 of the Specification, to provide details of processes by which torasemide can be produced and provides the chemical structural name for torasemide as well as stating its crystalline form (see column 11, 16-24) and its melting point (see column 14, lines 29-33).

Applicants submit that the amendment to the Specification does not introduce new matter because the amendment merely sets forth an inherent property of torasemide that would be known to one skilled in the art, such as by reference to the Scheen and Lesne publications listed in paragraph 7 of the instant Specification and which themselves reference the Delarge and

LaPiere reference (Annales pharmaceutiques françaises (1978) 36:369-380) which describes the compound torasemide. Furthermore, the Specification's specific reference to US 4,018,929 is meant to identify the torasemide chemical structure and properties.

According to MPEP § 2163.07(a) entitled "Inherent Function, Theory, or Advantage – 2100 Patentability," entry of this amendment is fully proper and does not introduce new matter. MPEP § 2163.07(a) states:

> By disclosing in a patent application a device that inherently performs a function or has a property, operates according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter. *In re Reynolds*, 443 F.2d 384, 170 USPQ 94 (CCPA 1971); *In re Smythe*, 480 F. 2d 1376, 178 USPQ 279 (CCPA 1973). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).

Furthermore, the courts have recognized that addition of inherent properties of material adequately disclosed in the original disclosure, as was torasemide, is appropriate (see, *Ex parte Davisson and Finlay*, 133 USPQ 400, 402 (BPAI 1958) as well as *In re Nathan, Hogg and Schneider*, 140 USPQ 601 (CCPA 1964). Consequently, Applicants properly request entry of the amendment into the Specification as no new matter is present.

Claim Rejections – 35 USC § 103

Maegerlein et al. in view of Tian et al.

The Examiner has rejected claims 1-5 and 7-15 as unpatentable over Maegerlein *et al.* as evidenced by Azarmi *et al.* in view of Tian *et al.* The Examiner contends that Maegerlein *et al.* exemplify a tablet comprising torasemide present in 5%, Eudragit RL present in 4% and crosscarmelose present in 2.5% and also containing customary pharmacologically acceptable

excipients. The Examiner acknowledges that Maegerlein *et al.* do not teach the addition of lactose. Here the Examiner contends that Tian *et al.* provide this component. Tian *et al.* describe a tablet core containing lactose as a diluent and which is then coated to effect a gradual release of the active ingredient. Applicants respectively traverse.

As a preliminary matter, Applicants note that claims 3-6 and 9-10 have been canceled, making the rejections based upon these claims moot.

Applicants next note that Maegerlein *et al.* state in paragraph [0001], lines 1-3 of the Specification:

> The present invention relates to preparations of the active compound torasemide, in which the torasemide is present in essentially noncrystalline form. (emphasis added)

Similarly, paragraph [0008] reads:

> Accordingly, we have found that this object is achieved by storage-stable solid or semisolid preparations in which the torasemide is present in essentially noncrystalline form. Preferably, the preparations are a so-called "solid solution". The preparations, however, can also contain amorphous agglomerates dispersed homogeneously in the binder matrix, the size of such agglomerates preferably being in the region of $\leq 1\,\mu m$. (emphasis added)

Claim 1 also underscores this fact, stating:

> 1. A stable solid or semisolid pharmaceutical preparation, comprising torasemide in essentially noncrystalline form. (emphasis added)

That is, the torasemide present in the Maegerlein *et al.* compositions is not present in crystalline form, as it is in the instant invention, but instead is present in amorphous form. Consequently, the skilled artisan would not have turned to Maegerlein *et al.* to produce a tablet where the torasemide was in crystalline form and would not have had a reasonable expectation of success in so doing.

The Tian *et al.* reference does not fill the void left by Maegerlein *et al.* Therefore, the obviousness rejection based upon Maegerlein *et al.* in view of Tian *et al.* cannot stand. Applicants request removal of the rejection.

Maegerlein et al., Tian et al. and Pankhania et al.

The Examiner has rejected claim 6 as being unpatentable over Maegerlein *et al.* as evidenced by Azarmi *et al.* in view of Tian *et al.* and in further view of Pankhania *et al.* The Examiner's allegations regarding the combination of Maegerlein *et al.* and Tian *et al.* are set forth above. The Examiner cites Pankania *et al.* to contend that polymers known for possessing sustained release properties include xanthan gum, guar gum and acrylic resins and for teaching that one of these can replace another.

Applicants again note that claims 3-6 and 9-10 have been canceled, making the rejections based upon these claims moot.

As noted above, the combination of Maegerlein *et al.* and Tian *et al.* does not make the instant invention obvious because the claimed invention contains torasemide in crystalline form. The Pankhania *et al.* reference again does not cure the defects left by the combination of Maegerlein *et al.* and Tian *et al.* Consequently, Applicants request removal of the rejection.

Berner et al. and Kaplan

The Examiner has rejected claims 1-15 as unpatentable over Berner *et al.* in view of Kaplan. The Examiner alleges that Berner *et al.* is directed to a controlled release oral dosage form for the continuous, sustained administration of a pharmacologically active agent and teaches suitable polymers such as guar gum as well as torasemide and binders such as starch, sugars such as lactose and lubricants such as magnesium stearate. Applicants respectfully traverse.

Once again, Applicants note that claims 3-6 and 9-10 have been canceled, making the rejections based upon these claims moot.

Applicants submit that the Examiner fails to establish a *prima facie* case of obviousness from the cited references. In particular, the Examiner has impermissibly used hindsight to make the instant rejection, using the claims as a "template" upon which to assemble references, each reciting an element of the claim.

That the Examiner has used a "templating" approach to making the instant rejection is apparent from the vast number of active ingredients, polymers, binders, lubricants, disintegrants,

fillers, *etc.* presented in Berner *et al.* and the extraordinarily broad and superficial disclosure of torasemide drugs presented in the review article entitled "Diuretics as a Basis of Antihypertensive Therapy An Overview" authored by Kaplan. The Examiner relies upon Kaplan stating "... Berner *et al.* do not exemplify a formulation comprising torasemide. However, this deficiency is cured by Kaplan" (Office Action page 8, last paragraph). But there is no actual disclosure of a torasemide formulation in the Kaplan reference.

Kaplan merely states:

> Therefore, I strongly recommend the use of longer acting diuretics for those with good renal function and either metolazone[23] or perhaps torasemide[24] for those with impaired renal function who need stronger diuretics" (see page 23, right column, first full paragraph, second sentence).

Kaplan then simply recites a statement from the 1997 Sixth Report of the US Joint National Committee regarding what "the optimal formulation should provide (see page 23, right column, second full paragraph, second sentence). This type of disclosure hardly presents "a formulation comprising torasemide."

Such an approach to making an obviousness rejection has been repeatedly rebuked by the courts. See, e.g. *Sensonics, Inc. v. Aerosonic Corp.*, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996):

> To draw on hindsight knowledge of the patented invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction -- an illogical and inappropriate process by which to determine patentability. *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed.Cir. 1983). The invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have been perceived in the state of the art that existed at the time the invention was made. *Interconnect Planning Corp. v. Feil* , 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed.Cir. 1985).

It is not sufficient to establish *prima facie* obviousness by merely listing a set of references that together set forth each of the elements of the claim individually. A claim composed of several elements is not proved obvious simply by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). There must be a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *Id.* Unless the combined prior art references suggest the claimed invention, either explicitly or implicitly,

the Examiner must present a "*convincing line of reasoning* as to why one of ordinary skill in art would have found the claimed invention to have been obvious." *Ex parte Rorher,* Appeal 2009-001292, 5 (BPAI, February 5, 2010) *citing Ex parte Clapp,* 227 U.S.P.Q. 972, 973 (BPAI 1985)(emphasis added, internal quotations omitted).

Furthermore, the Examiner is not permitted to merely extract from cited references those teachings that support a conclusion of obviousness. Rather, the references *must be considered as a whole*. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303 (Fed. Cir. 1983):

> In its consideration of the prior art, however, the district court erred in ...considering the references in less than their entireties, i.e., in disregarding disclosures in the references that diverge from and teach away from the invention at hand. In re *Kuderna,* 426 F.2d 385, 165 USPQ 575 (CCPA 1970).

Since the Examiner has improperly used a "templating," hindsight-based approach to formulating the instant rejection, it is plain that the combination of Berner *et al.* and Kaplan fails to establish *prima facie* obviousness of instant claims 1, 2, 7, 8 and 11-23. Accordingly, the instant rejection should be withdrawn.

Conclusion

In view of the above remarks, all of the claims are submitted as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested. Applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Susan W. Gorman, Ph.D., Reg. No. 47,604 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $490.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: April 25, 2011

Respectfully submitted,

#47,604

By _____
Marc S. Weiner
Registration No.: 32,181
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Rd
Falls Church, VA 22042
(703) 205-8000
Attorney for Applicant

Enclosures: Entry 9690 (Torasemide) description from the Merck Index
Torasemide description from DrugBank
Torasemide description from Chemical Book